

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 96700/955		Date of mailing (day/month/year) 09 NOV 2005 FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/US05/13222	International filing date (day/month/year) 20 April 2005 (20.04.2005)	Priority date (day/month/year) 21 April 2004 (21.04.2004)
International Patent Classification (IPC) or both national classification and IPC IPC(7): A61K 35/14, 38/16 and US Cl.: 530/385; 514/6		
Applicant ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY		

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Date of completion of this opinion 18 October 2005 (18.10.2005)	Authorized officer Karen Cochrane Carlson, Ph.D. Telephone No. 571-272-0700
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Form PCT/ISA/237 (cover sheet) (April 2005)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US05/13222

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
- ☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
- ☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
- ☐ filed together with the international application in electronic form.
- ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
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International application No.

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-5, 18, 19, 29, 30, 33, 34 and 37-40

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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>40</u>	YES
	Claims <u>1-5, 18, 19, 29, 30, 33, 34, 37-39</u>	NO
Inventive step (IS)	Claims <u>40</u>	YES
	Claims <u>1-5, 18, 19, 29, 30, 33, 34, 37-39</u>	NO
Industrial applicability (IA)	Claims <u>1-5, 18, 19, 29, 30, 33, 34, 37-40</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-3 and 18 lack novelty under PCT Article 33(2) as being anticipated by DAS et al. (US Patent 3,964,865).
DAS et al. teach lyophilized or powdered hemoglobin that is stable. This hemoglobin is more than 99% oxidized to met-hemoglobin (Example 1), indicating that oxygenated hemoglobin remains in lyophilized solution.

Claims 1-5, 18, 19, 29, 30, 33, 34, and 37-39 lack novelty under PCT Article 33(2) as being anticipated by HELLER et al. (1999; J. Pharmaceutical Sciences 88(1): 58-64).

HELLER et al. teach lyophilized or powdered hemoglobin (Claims 1, 18). The hemoglobin was pegylated (Claim 4) with one or two PEG molecules (Page 60, right column, lines 8-9), each PEG having an average molecular weight of 3350 D (page 59, right column, line 31 Claims 37-39). The pegylated hemoglobin reduces loss of structure (abstract; page 64, right column) and therefore the pegylated hemoglobin is more stable (Claims 2, 3).

Claims 5, 29, 30, 19, 33, and 34) are included in this rejection because the structure of the independent claims appear to be the same, and thus include met-hemoglobin even though this variable was not assessed by HELLER et al.

Claims 1-5, 18, 19, 29, 30, 33, 34, and 37-40 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.